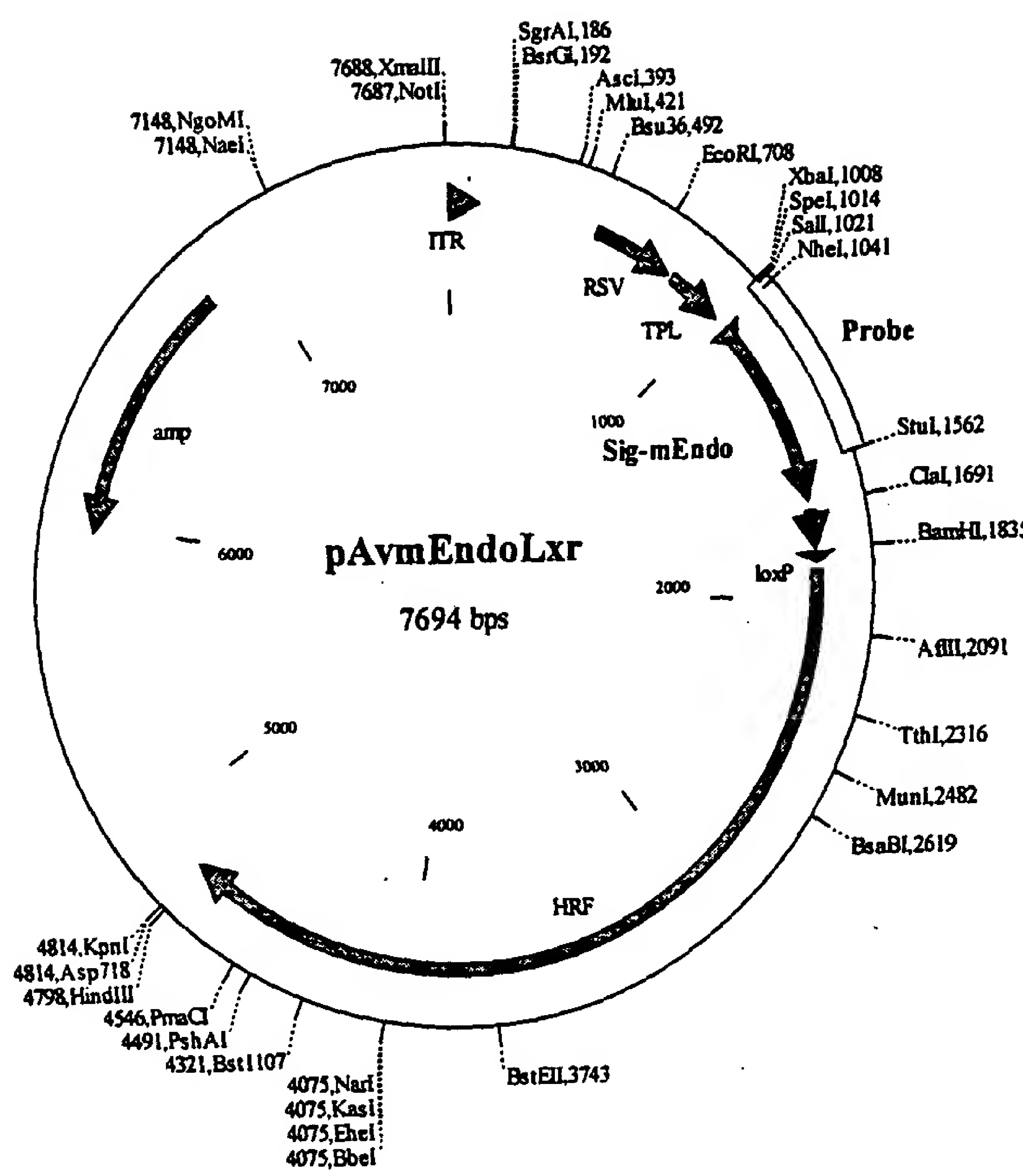

SgrAI,186
BsrGI,192
AscI,393
MluI,421
Bsu36,492
EcoRI,708
XbaI,1008
SpeI,1014
SalI,1021
NheI,1041
7688,XmaIII
7687,NotI
7148,NgoMI
7148,NaeI
ITR
RSV
TPL
Probe
amp
7000
1000
Sig-mEndo
StuI,1562
ClaI,1691
BamHI,1835
pAvmEndoLxr
7694 bps
6000
2000
loxP
AflII,2091
TthI,2316
MunI,2482
BsaBI,2619
5000
3000
4000
HRF
4814,KpnI
4814,Asp718
4798,HindIII
4546,PmaCI
4491,PshAI
4321,Bst1107
4075,NarI
4075,KasI
4075,EheI
4075,BbeI
BstEII,3743

Fig. 1A

```
ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGG 42
 M  E  T  D  T  L  L  L  W  V  L  L  L  W

GTTCCAGGTTCCACTGGTGACGCGGCCCATACTCATCAGGAC 84
 V  P  G  S  T  G  D  A  A  H  T  H  Q  D

TTTCAGCCAGTGCTCCACCTGGTGGCACTGAACACCCCCCTG 126
 F  Q  P  V  L  H  L  V  A  L  N  T  P  L

TCTGGAGGCATGCGTGGTATCCGTGGAGCAGATTTCCAGTGC 168
 S  G  G  M  R  G  I  R  G  A  D  F  Q  C

TTCCAGCAAGCCCGAGCCGTGGGGCTGTCGGGCACCTTCCGG 210
 F  Q  Q  A  R  A  V  G  L  S  G  T  F  R

GCTTTCCTGTCCTCTAGGCTGCAGGATCTCTATAGCATCGTG 252
 A  F  L  S  S  R  L  Q  D  L  Y  S  I  V

CGCCGTGCTGACCGGGGGTCTGTGCCCATCGTCAACCTGAAG 294
 R  R  A  D  R  G  S  V  P  I  V  N  L  K

GACGAGGTGCTATCTCCCAGCTGGGACTCCCTGTTTTCTGGC 336
 D  E  V  L  S  P  S  W  D  S  L  F  S  G

TCCCAGGGTCAAGTGCAACCCGGGGCCCGCATCTTTTCTTTT 378
 S  Q  G  Q  V  Q  P  G  A  R  I  F  S  F

GACGGCAGAGATGTCCTGAGACACCCAGCCTGGCCGCAGAAG 420
 D  G  R  D  V  L  R  H  P  A  W  P  Q  K

AGCGTATGGCACGGCTCGGACCCCAGTGGGCGGAGGCTGATG 462
 S  V  W  H  G  S  D  P  S  G  R  R  L  M

GAGAGTTACTGTGAGACATGGCGAACTGAAACTACTGGGGCT 504
 E  S  Y  C  E  T  W  R  T  E  T  T  G  A

ACAGGTCAGGCCTCCTCCCTGCTGTCAGGCAGGCTCCTGGAA 546
 T  G  Q  A  S  S  L  L  S  G  R  L  L  E

CAGAAAGCTGCGAGCTGCCACAACAGCTACATCGTCCTGTGC 588
 Q  K  A  A  S  C  H  N  S  Y  I  V  L  C

ATTGAGAATAGCTTCATGACCTCTTTCTCCAAATAG 624
 I  E  N  S  F  M  T  S  F  S  K  .
```

Fig. 1B

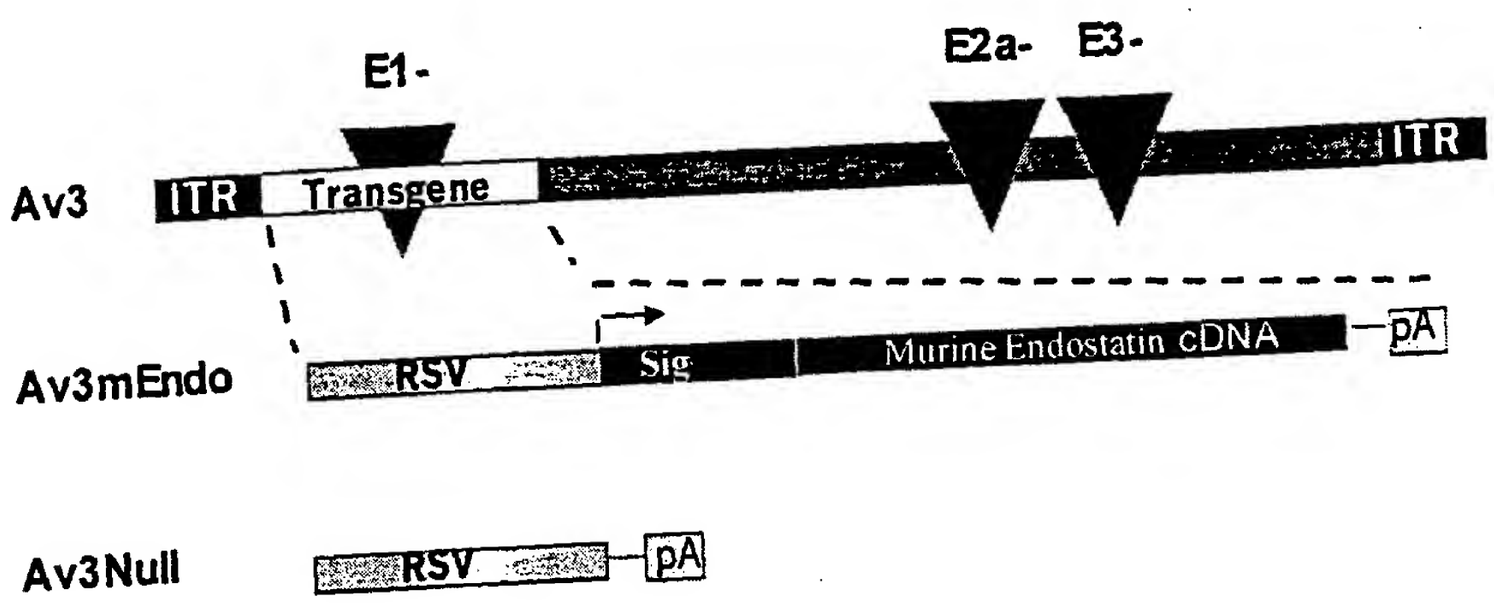


Fig. 2

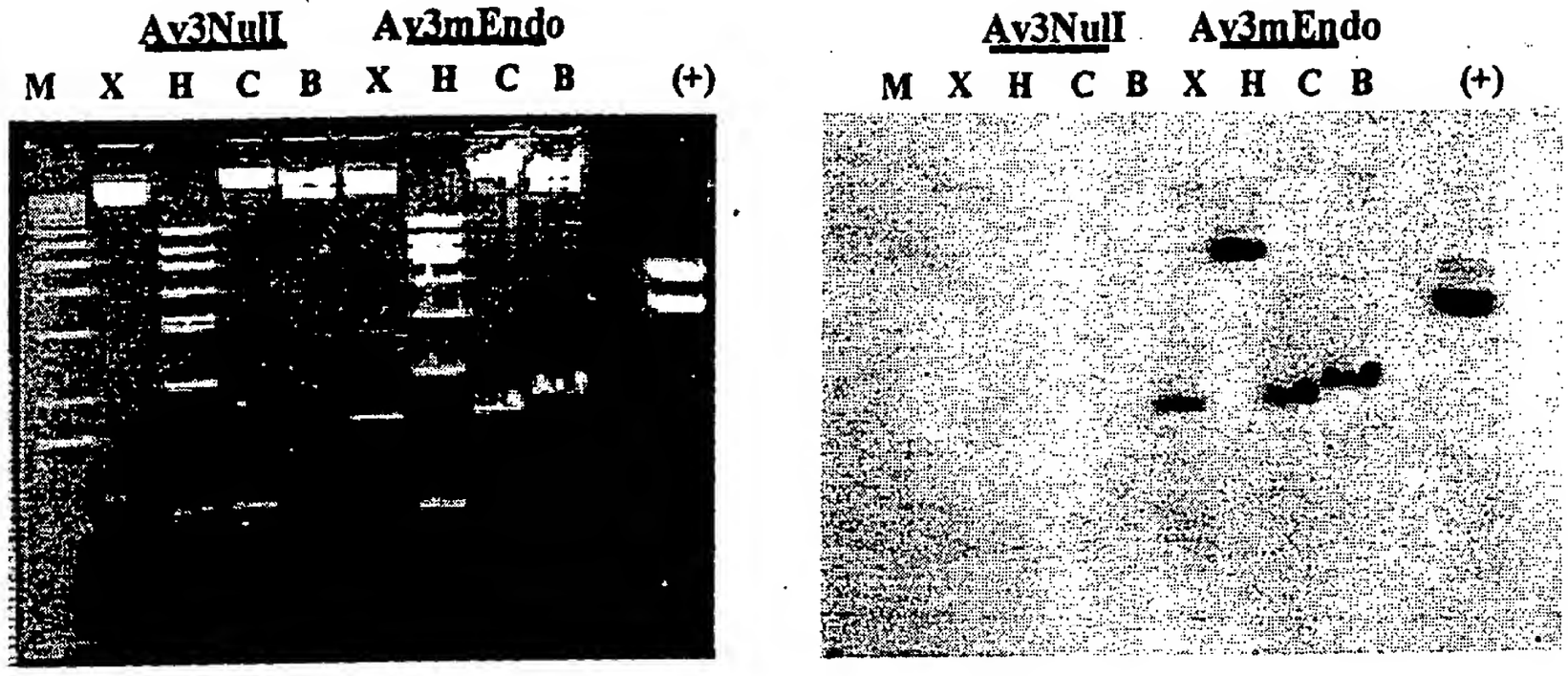


Fig. 3

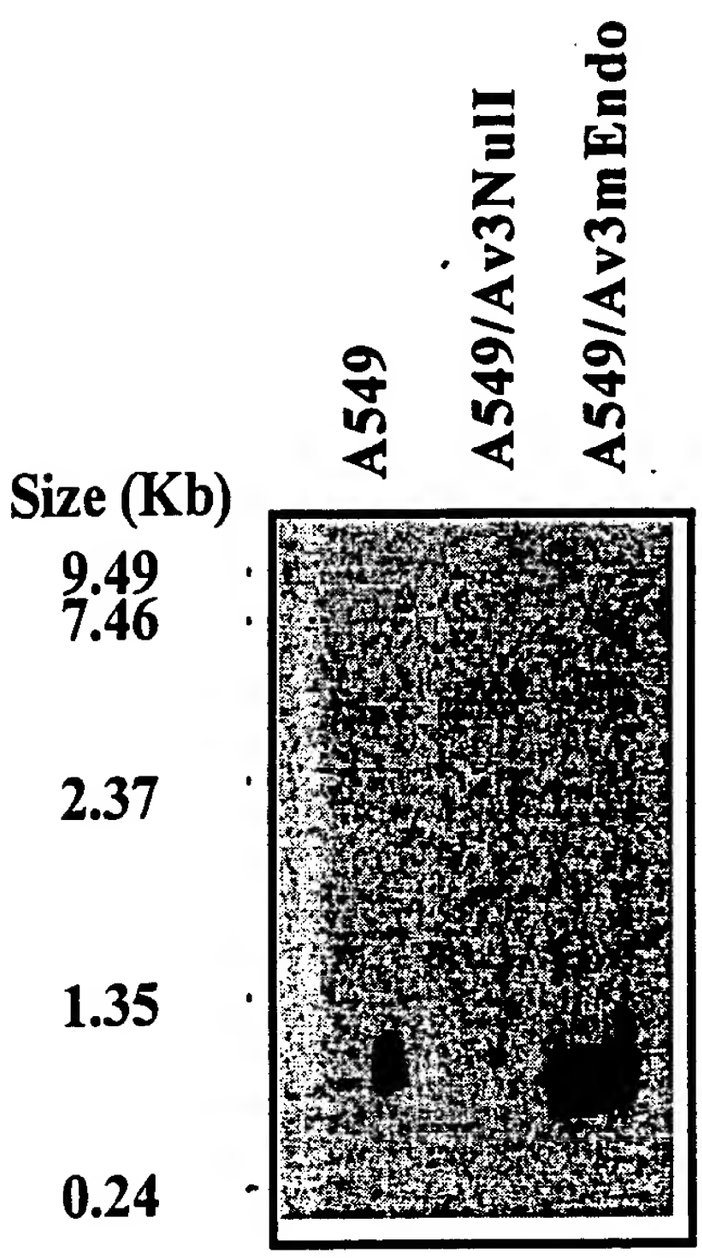


Fig. 4

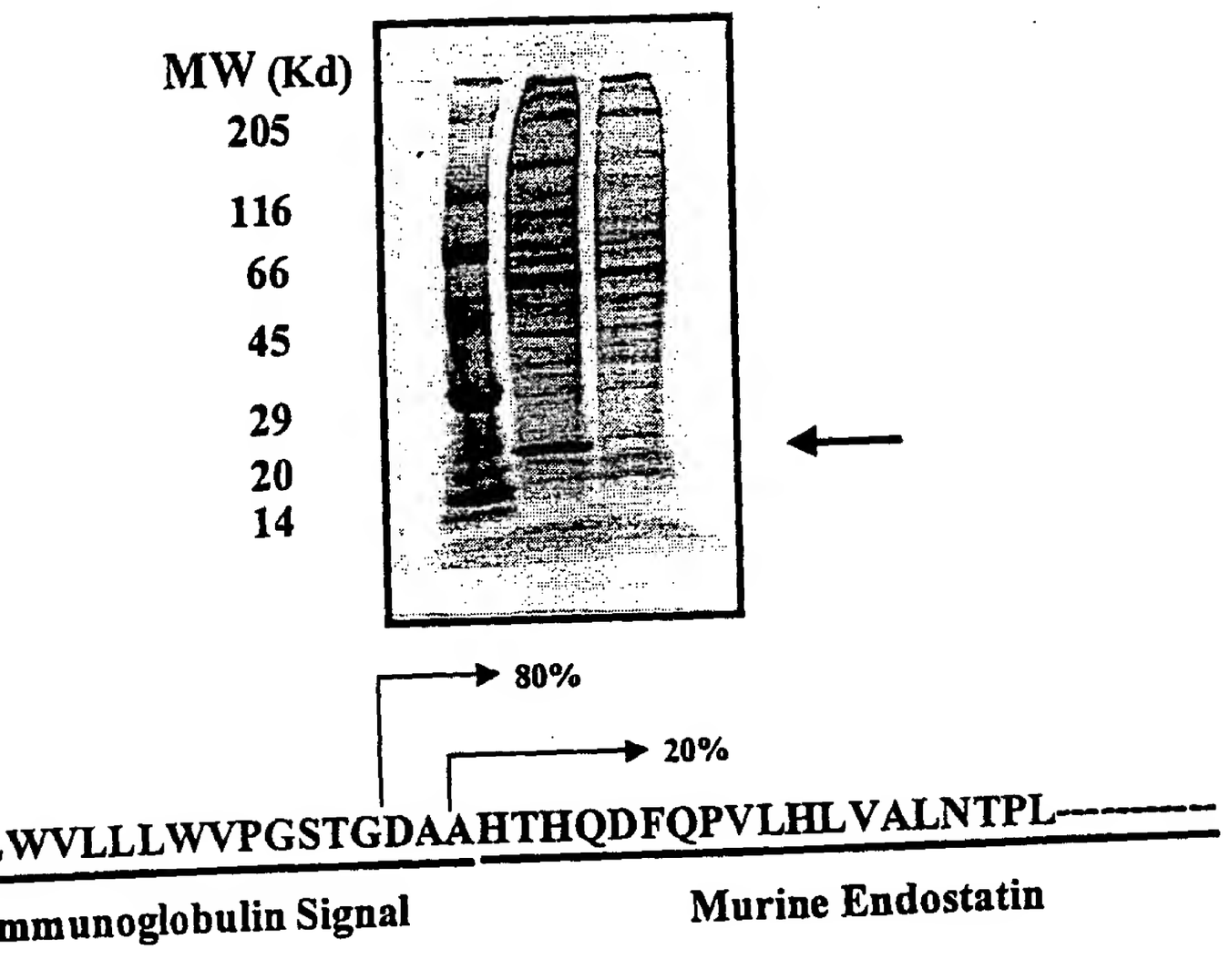

MW (Kd)
205
116
66
45
29
20
14
80%
20%
METDTLLLWVLLLWVPGSTGDAAHTHQDFQPVLHLVALNTPL
Murine Immunoglobulin Signal
Murine Endostatin

Fig. 5

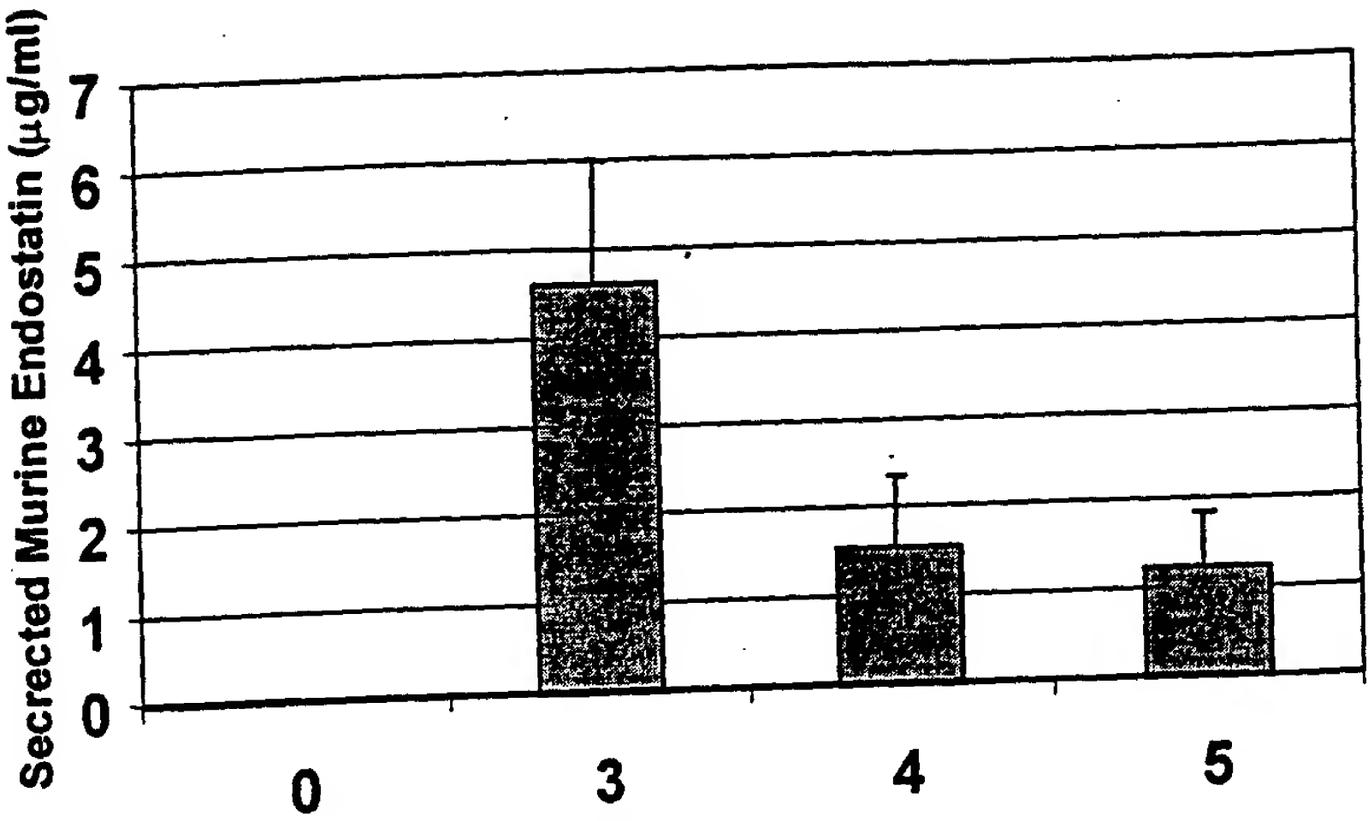

Secrected Murine Endostatin (µg/ml)
0
1
2
3
4
5
6
7
0
3
4
5
Day post transduction

Fig. 6

VEGF165 Induced HUVEC Migration

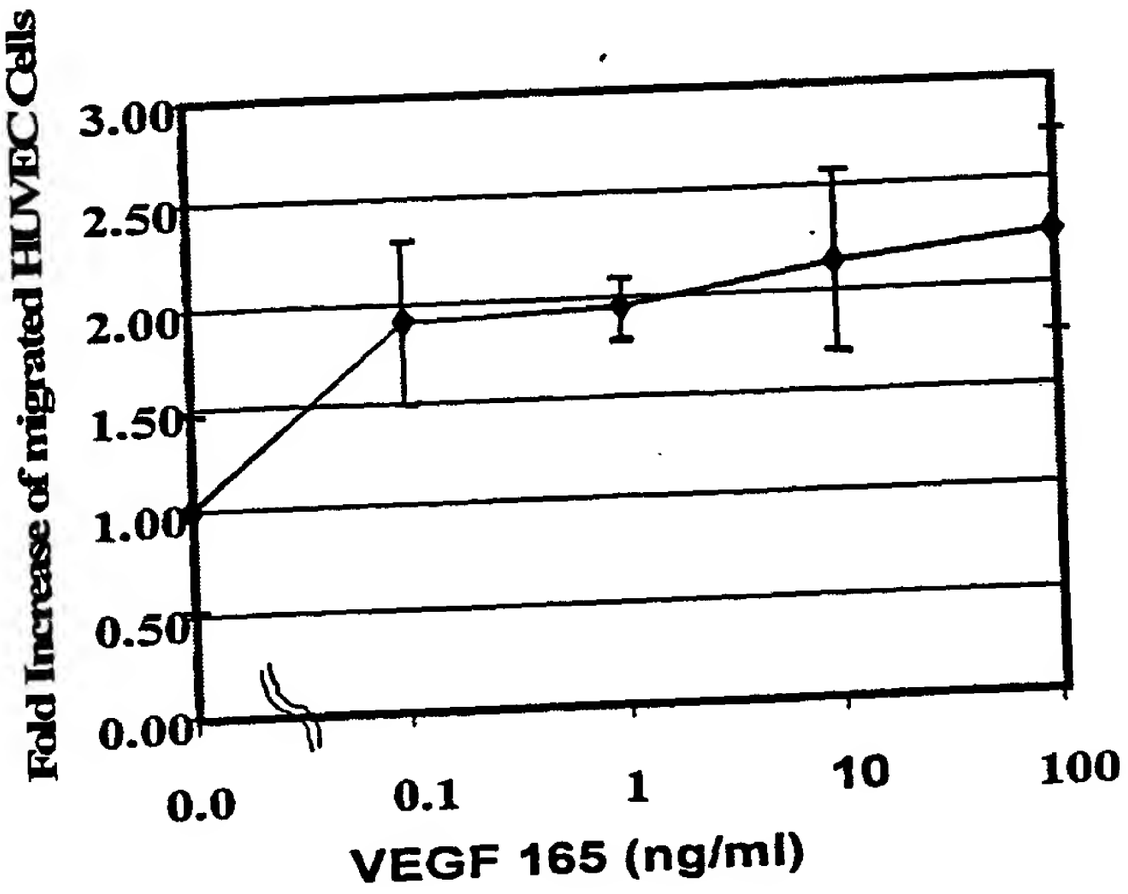
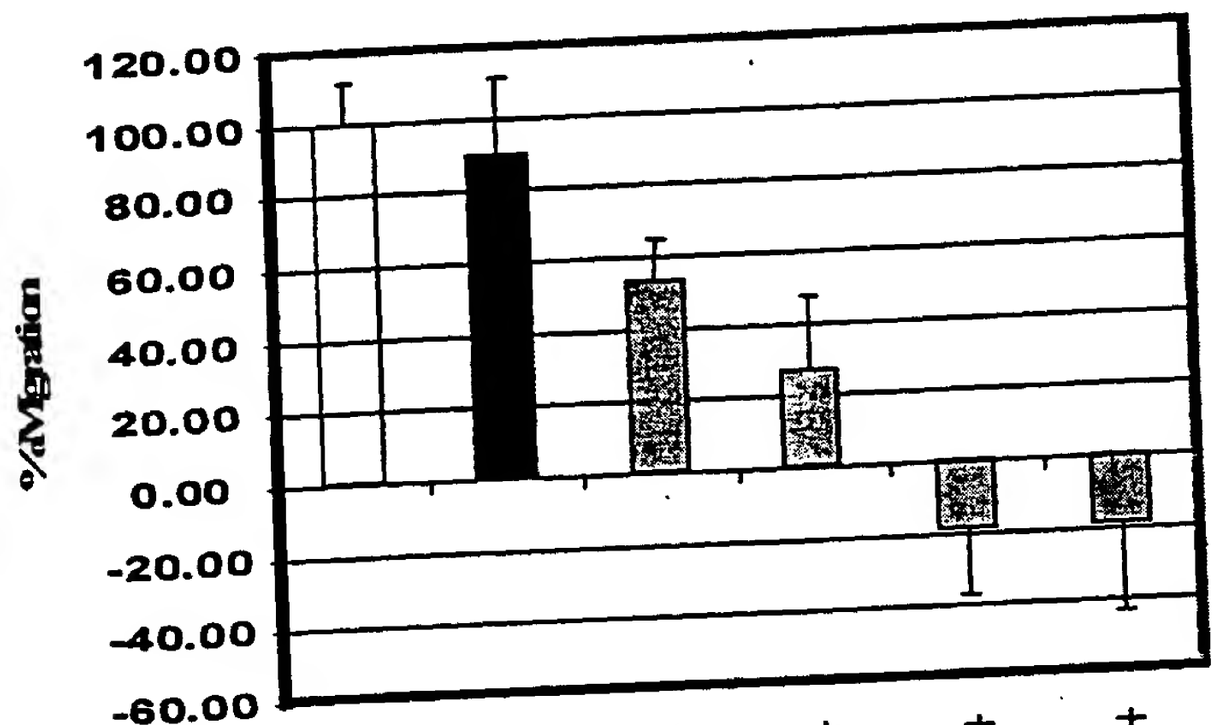


Fig. 7A

mEndo from Av3mEndo transduced S8



VEGF-165 (10 ng/ml)	+	+	+	+	+	+
NulI protein (100 ng/ml)	-	+	-	-	-	-
mEndo Protein (ng/ml)	-	-	0.1	1	10	100

Fig. 7B

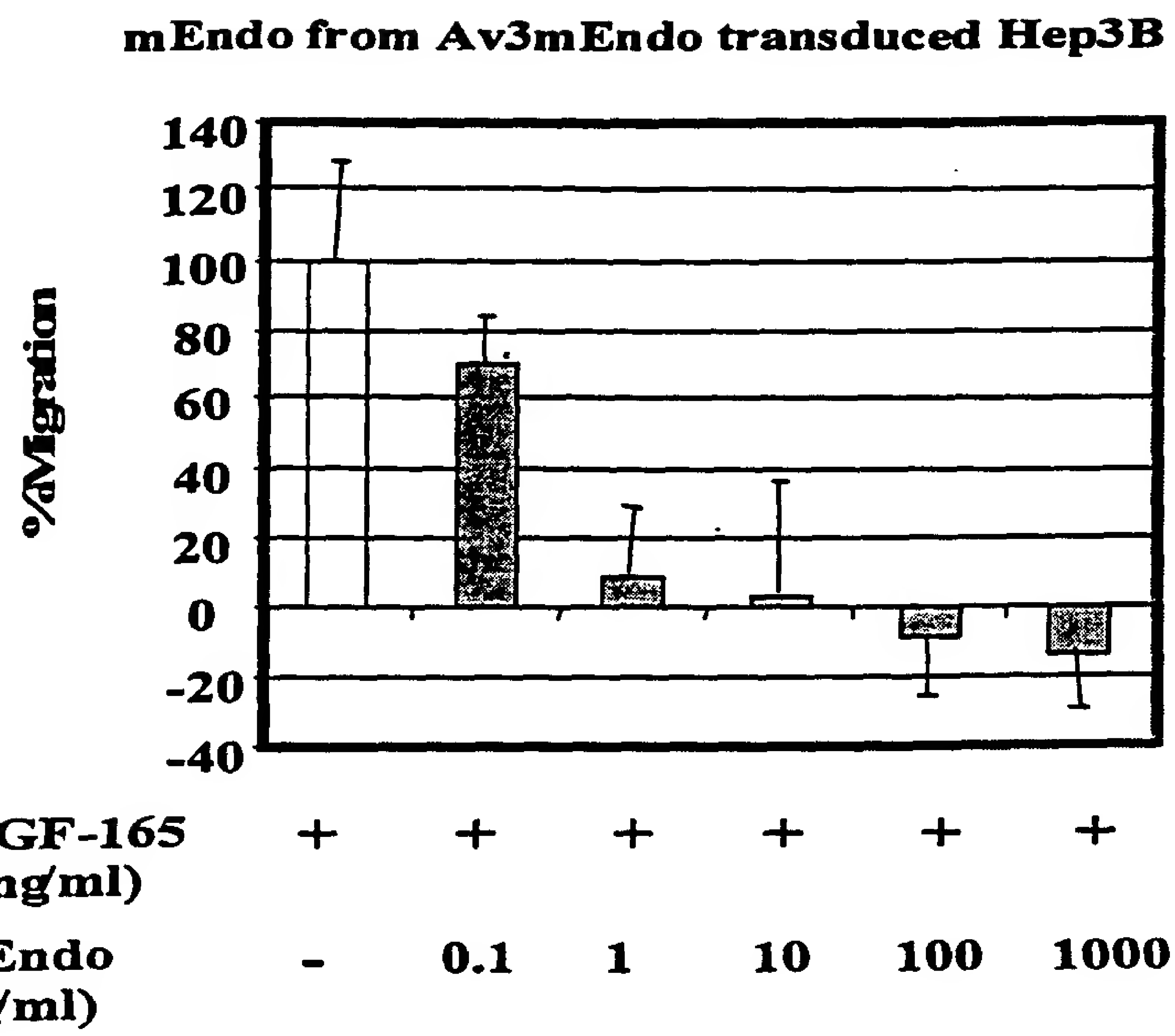

mEndo from Av3mEndo transduced Hep3B
%Migration
140
120
100
80
60
40
20
0
-20
-40
VEGF-165 (10ng/ml) + + + + + +
mEndo (ng/ml) - 0.1 1 10 100 1000

Fig. 7C

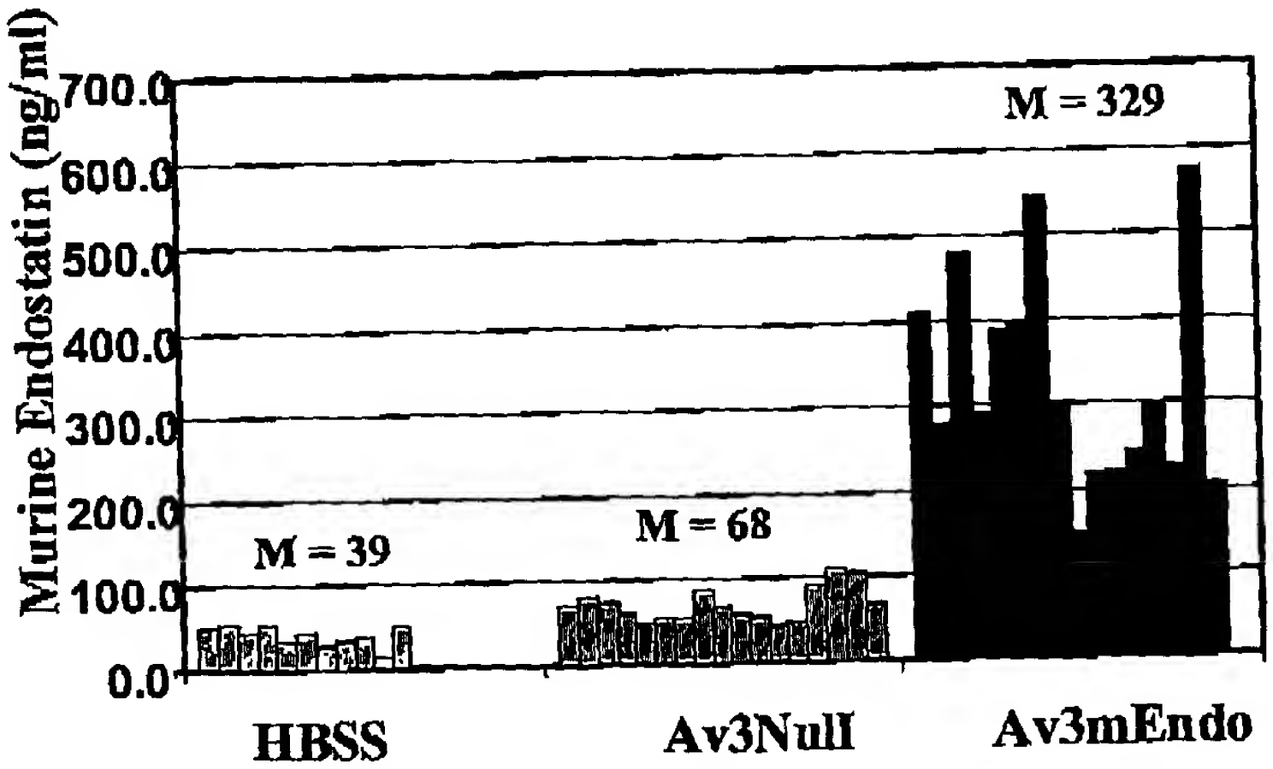

Murine Endostatin (ng/ml)
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
M = 39
M = 68
M = 329
HBSS
Av3Null
Av3mEndo

Fig. 8A

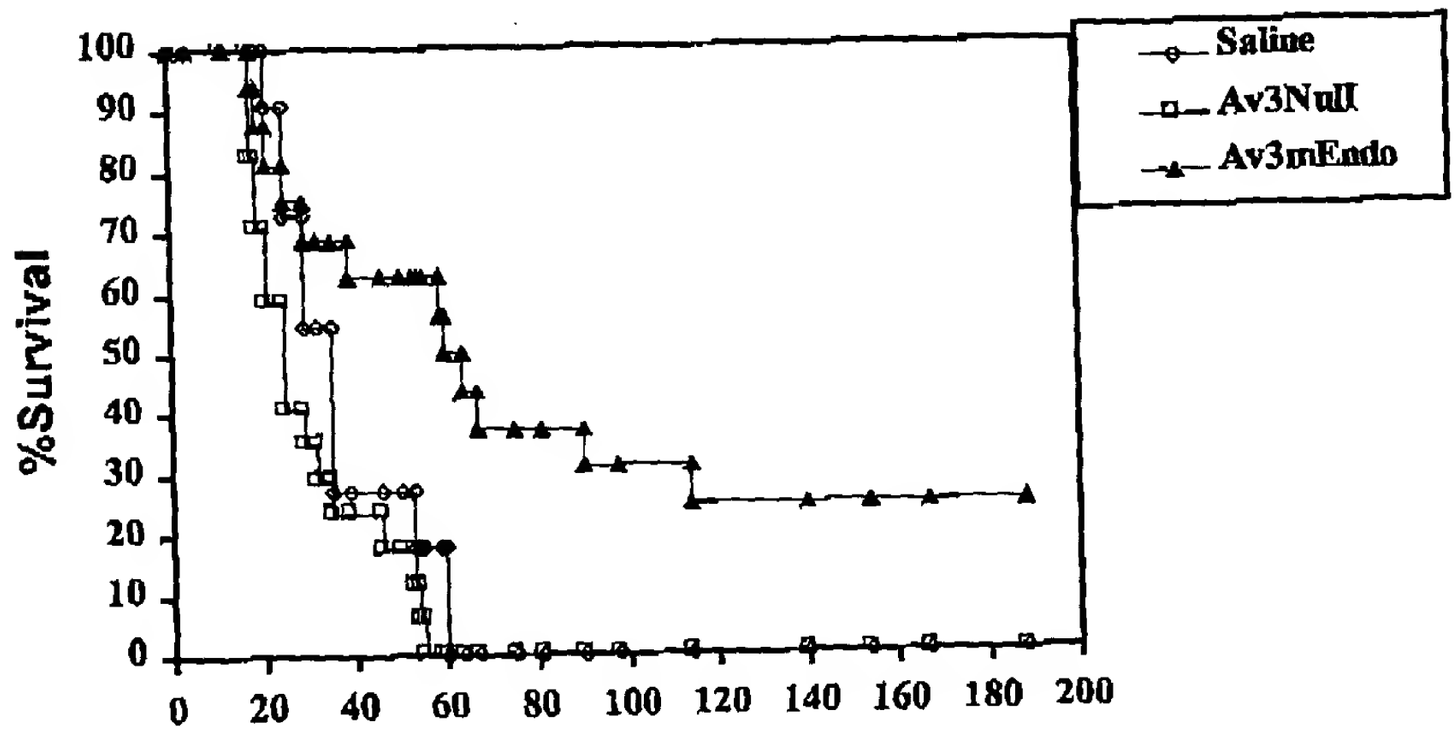

%Survival
100
90
80
70
60
50
40
30
20
10
0
0 20 40 60 80 100 120 140 160 180 200
Days post tumor implantation
Saline
Av3Null
Av3mEndo

Fig. 8B

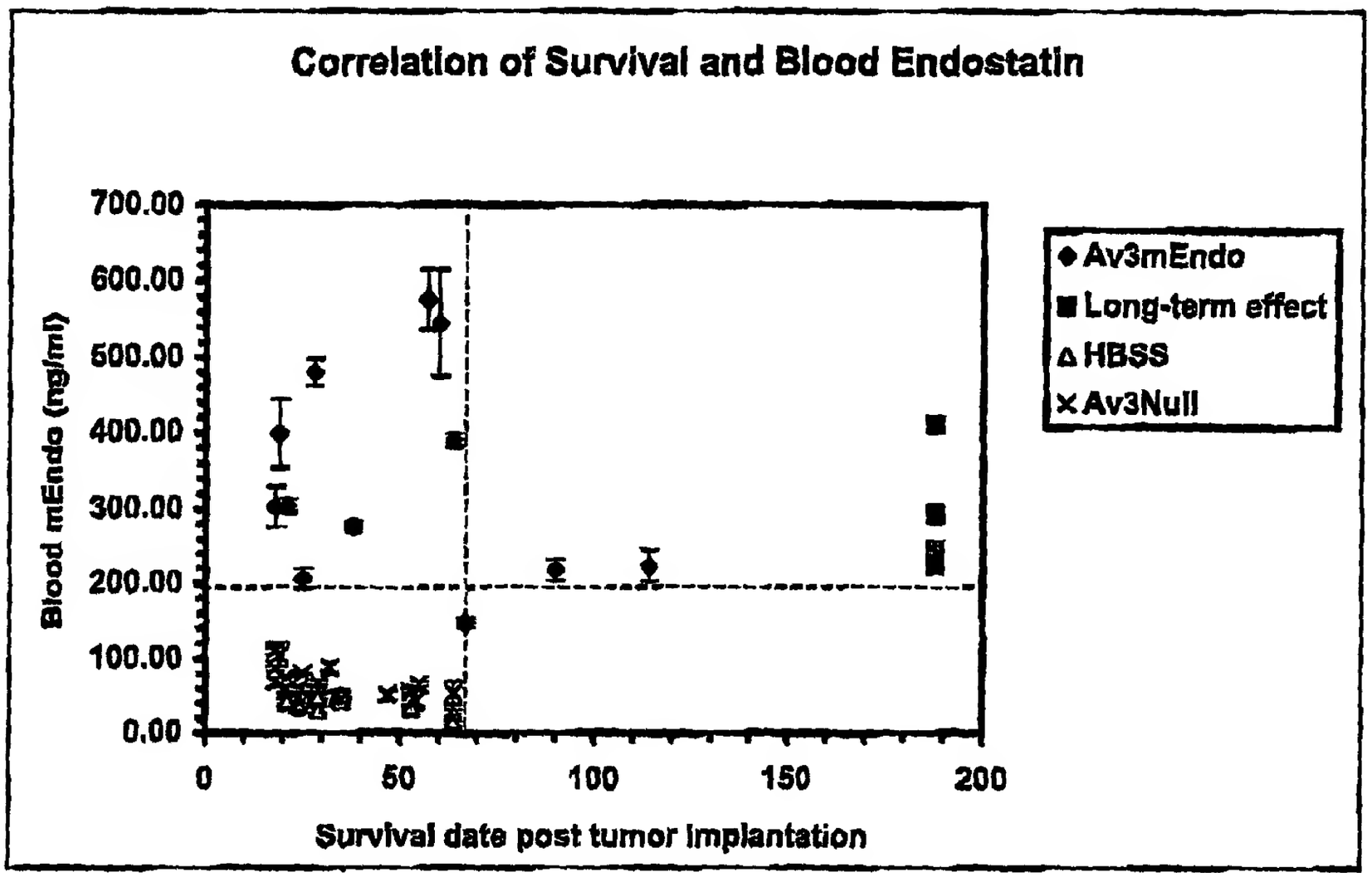
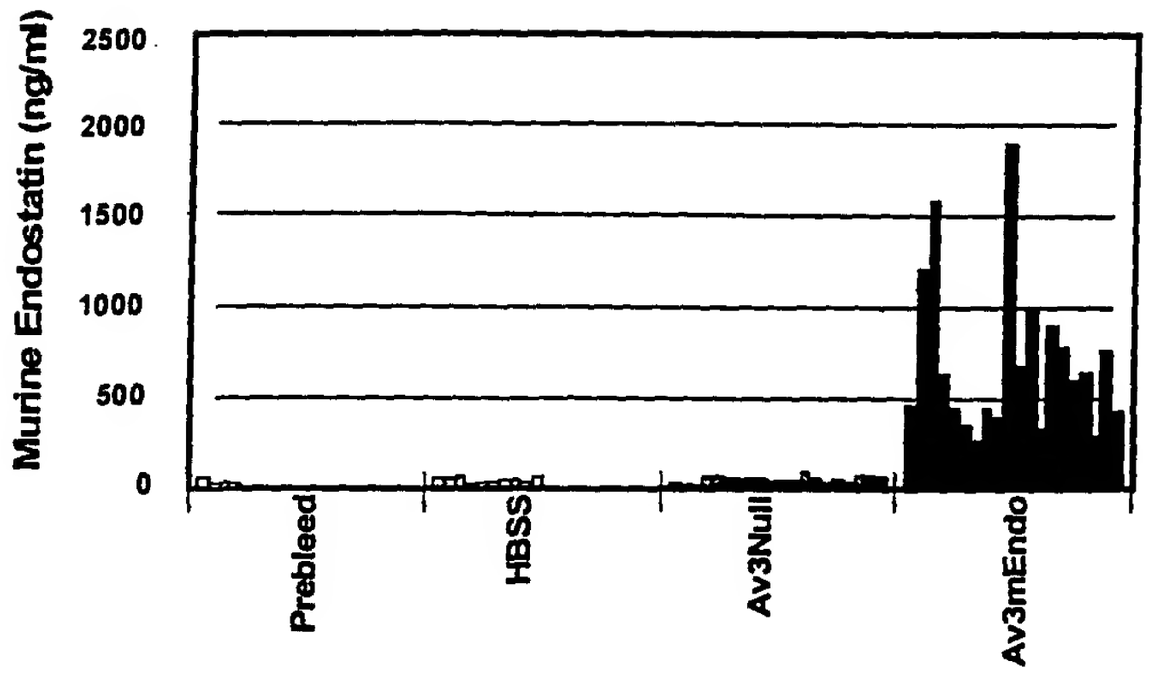

Correlation of Survival and Blood Endostatin
Blood mEndo (mg/ml)
700.00
600.00
500.00
400.00
300.00
200.00
100.00
0.00
0
50
100
150
200
Survival date post tumor implantation
Av3mEndo
Long-term effect
HBSS
Av3Null

Figure 8C

(A)


Murine Endostatin (ng/ml)
2500
2000
1500
1000
500
0
Prebleed
HBSS
Av3Null
Av3mEndo
Vector Transduced Mice

(B)

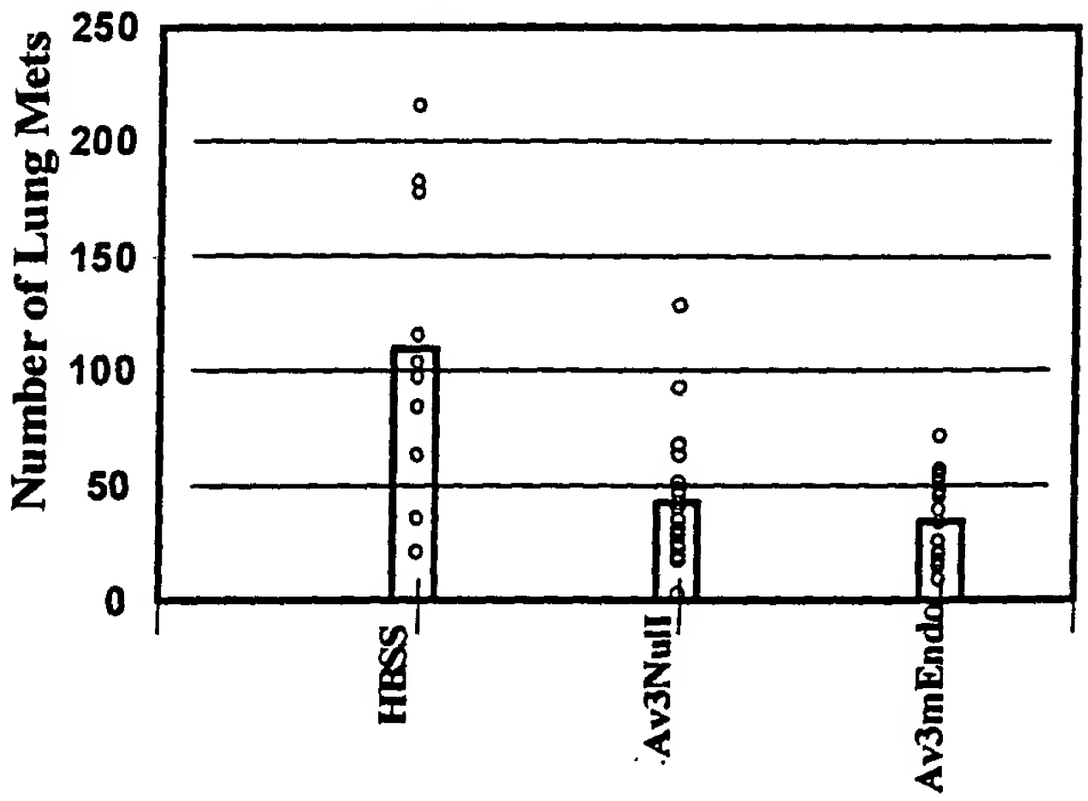

Number of Lung Mets
250
200
150
100
50
0
HBSS
Av3Null
Av3mEndo

Fig. 9

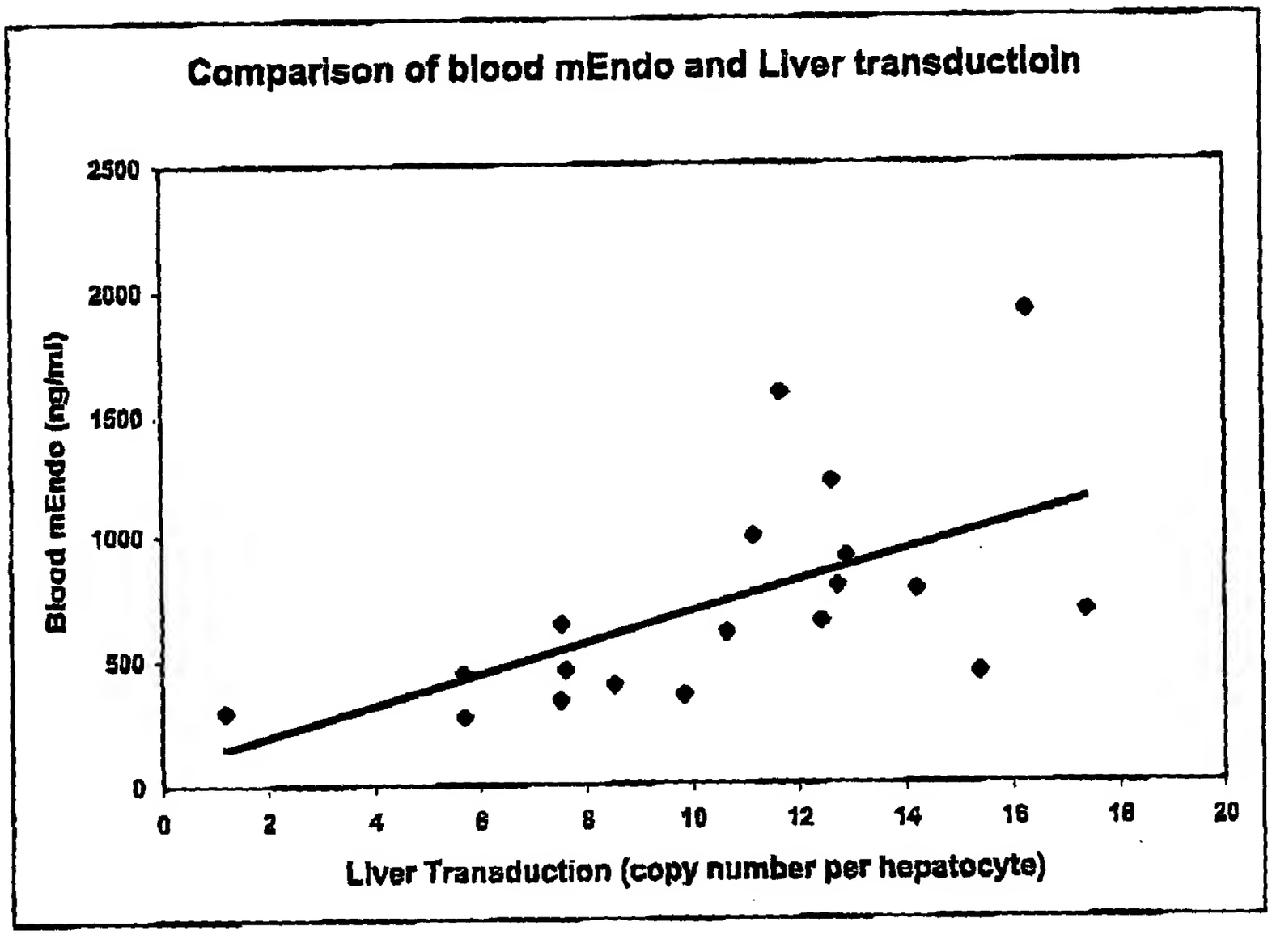

Comparison of blood mEndo and Liver transductioin
Blood mEndo (ng/ml)
2500
2000
1500
1000
500
0
0
2
4
6
8
10
12
14
16
18
20
Liver Transduction (copy number per hepatocyte)

Fig. 9C

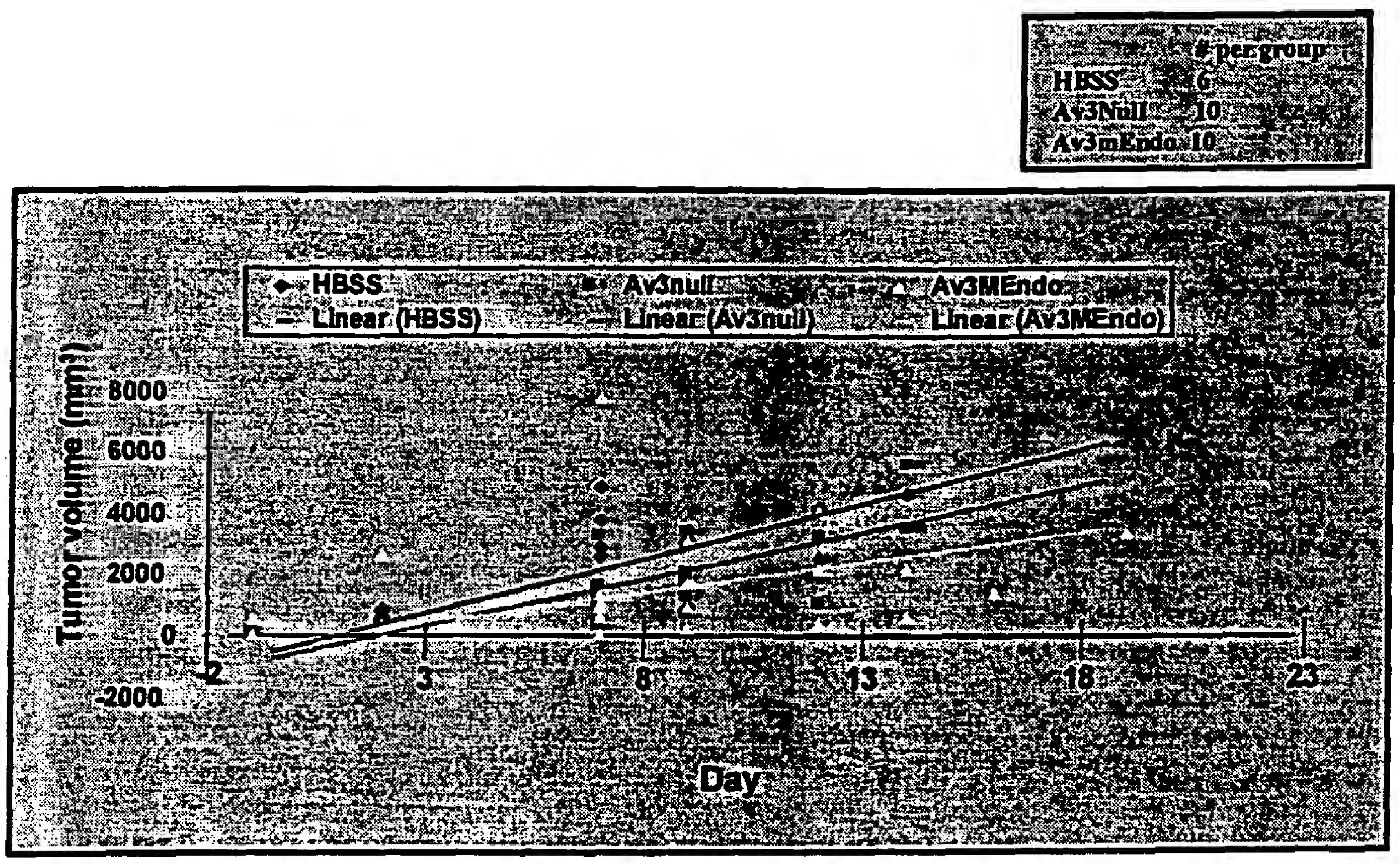


Fig. 10A

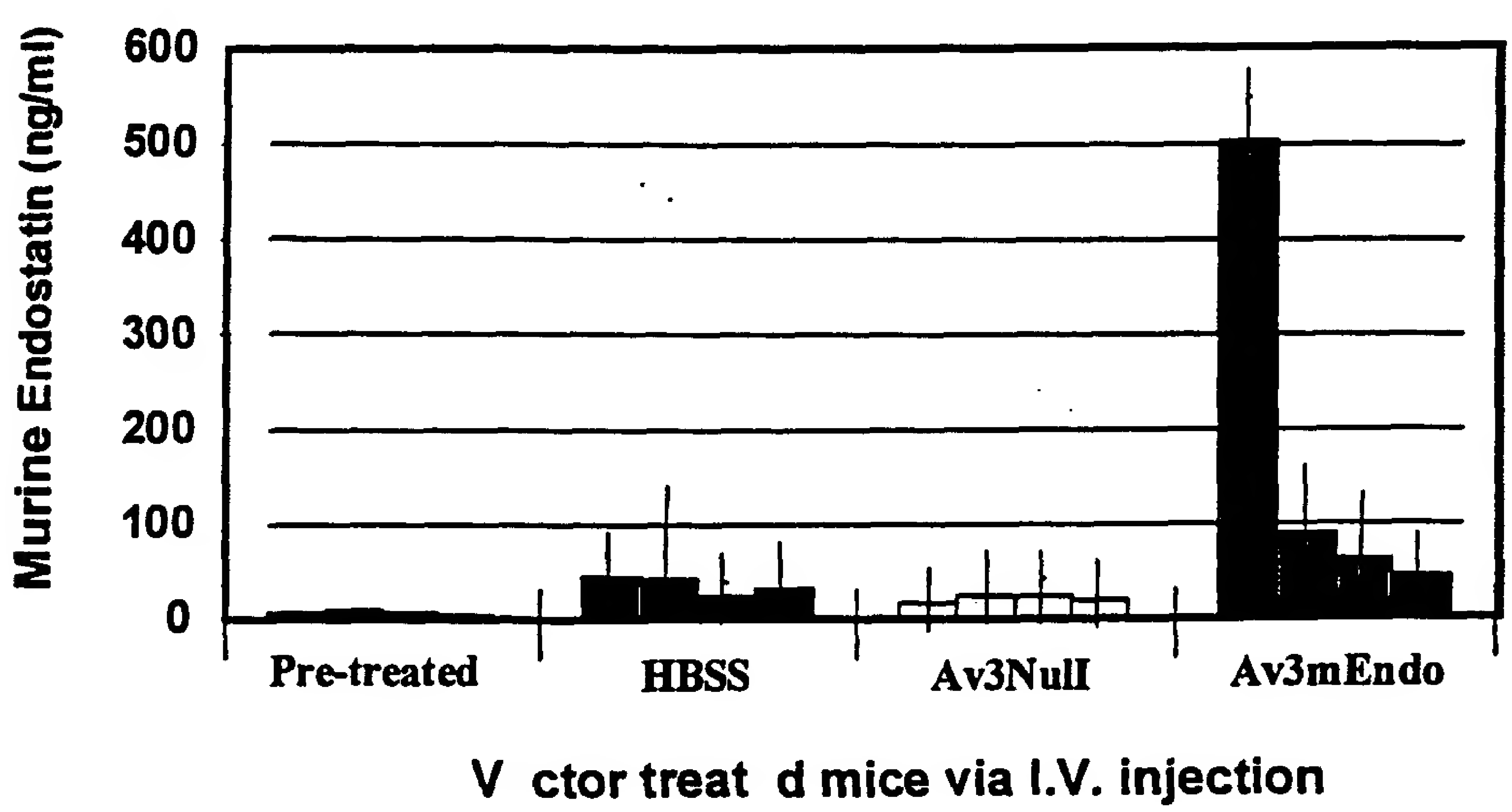


Fig. 10B

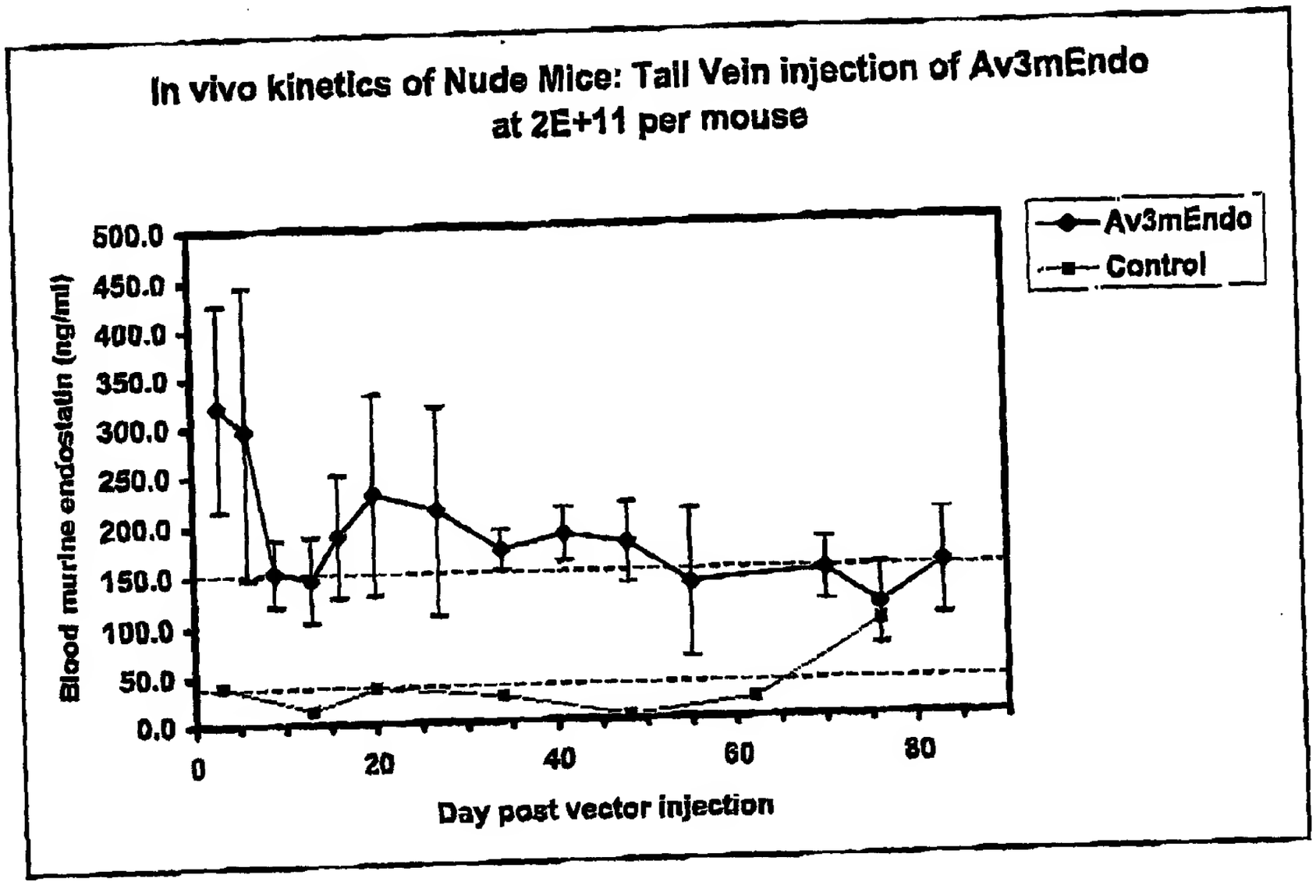

In vivo kinetics of Nude Mice: Tail Vein injection of Av3mEndo at 2E+11 per mouse
Blood murine endostatin (ng/ml)
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
0
20
40
60
80
Day post vector injection
Av3mEndo
Control

Fig. 11

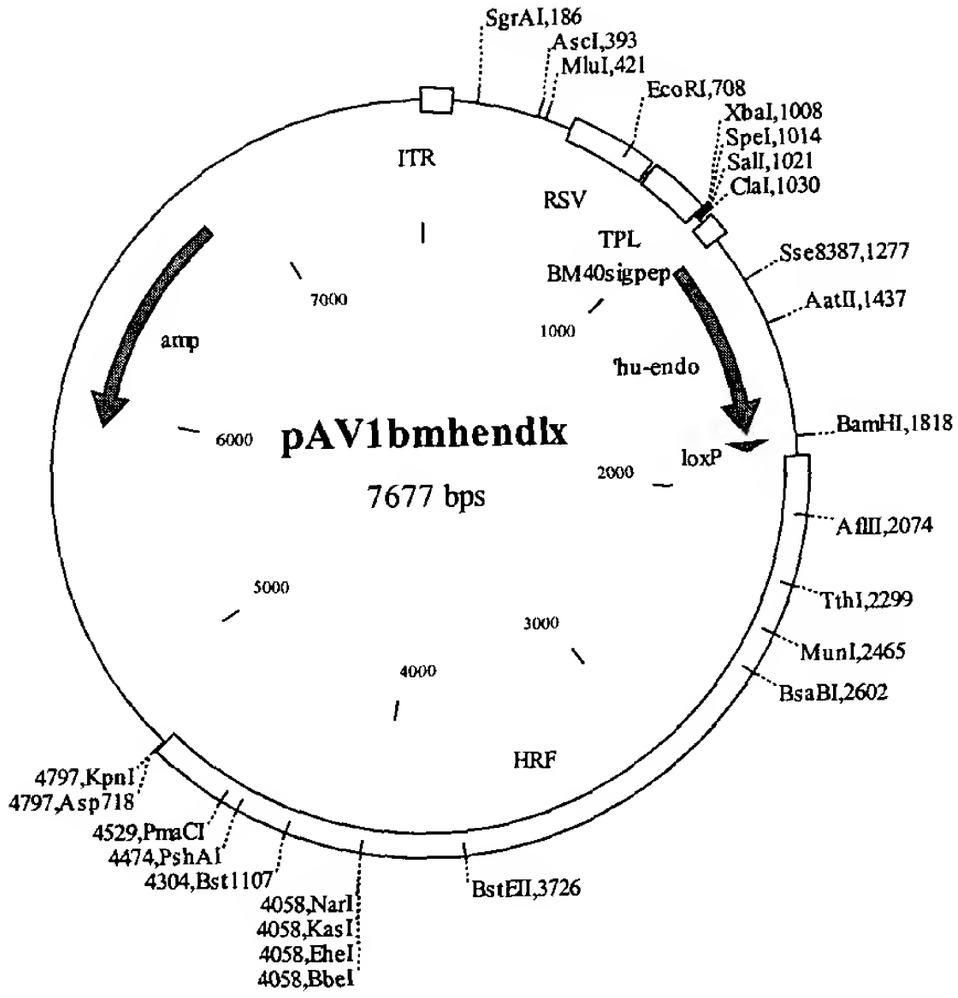

SgrAI,186
AscI,393
MluI,421
EcoRI,708
XbaI,1008
SpeI,1014
SalI,1021
ClaI,1030
Sse8387,1277
AatII,1437
BamHI,1818
AflII,2074
TthI,2299
MunI,2465
BsaBI,2602
BstEII,3726
4058,NarI
4058,KasI
4058,EheI
4058,BbeI
4304,Bst1107
4474,PshAI
4529,PmaCI
4797,Asp718
4797,KpnI
ITR
RSV
TPL
BM40sigpep
hu-endo
loxP
HRF
amp
pAV1bmhendlx
7677 bps
1000
2000
3000
4000
5000
6000
7000

Fig. 12A

```
ATGAGGGCCTGGATCTTCTTTCTCCTTTGCCTGGCCGGGAGG          42
 M  R  A  W  I  F  F  L  L  C  L  A  G  R

GCTCTGGCAGCCCCTCAGCAAGAAGCGCTCGCTCACAGCCAC          84
 A  L  A  A  P  Q  Q  E  A  L  A  H  S  H

CGCGACTTCCAGCCGGTGCTCCACCTGGTTGCGCTCAACAGC         126
 R  D  F  Q  P  V  L  H  L  V  A  L  N  S

CCCCTGTCAGGCGGCATGCGGGGCATCCGCGGGGCCGACTTC         168
 P  L  S  G  G  M  R  G  I  R  G  A  D  F

CAGTGCTTCCAGCAGGCGCGGGCCGTGGGGCTGGCGGGCACC         210
 Q  C  F  Q  Q  A  R  A  V  G  L  A  G  T

TTCCGCGCCTTCCTGTCCTCGCGCCTGCAGGACCTGTACAGC         252
 F  R  A  F  L  S  S  R  L  Q  D  L  Y  S

ATCGTGCGCCGTGCCGACCGCGCAGCCGTGCCCATCGTCAAC         294
 I  V  R  R  A  D  R  A  A  V  P  I  V  N

CTCAAGGACGAGCTGCTGTTTCCCAGCTGGGAGGCTCTGTTC         336
 L  K  D  E  L  L  F  P  S  W  E  A  L  F

TCAGGCTCTGAGGGTCCGCTGAAGCCCGGGGCACGCATCTTC         378
 S  G  S  E  G  P  L  K  P  G  A  R  I  F

TCCTTTGACGGCAAGGACGTCCTGAGGCACCCCACCTGGCCC         420
 S  F  D  G  K  D  V  L  R  H  P  T  W  P

CAGAAGAGCGTGTGGCATGGCTCGGACCCCAACGGGCGCAGG         462
 Q  K  S  V  W  H  G  S  D  P  N  G  R  R

CTGACCGAGAGCTACTGTGAGACGTGGCGGACGGAGGCTCCC         504
 L  T  E  S  Y  C  E  T  W  R  T  E  A  P

TCGGCCACGGGCCAGGCCTCCTCGCTGCTGGGGGGCAGGCTC         546
 S  A  T  G  Q  A  S  S  L  L  G  G  R  L

CTGGGGCAGAGTGCCGCGAGCTGCCATCACGCCTACATCGTG         588
 L  G  Q  S  A  A  S  C  H  H  A  Y  I  V

CTCTGCATTGAGAACAGCTTCATGACTGCCTCCAAGTAG            627
 L  C  I  E  N  S  F  M  T  A  S  K  .
```

Fig. 12B

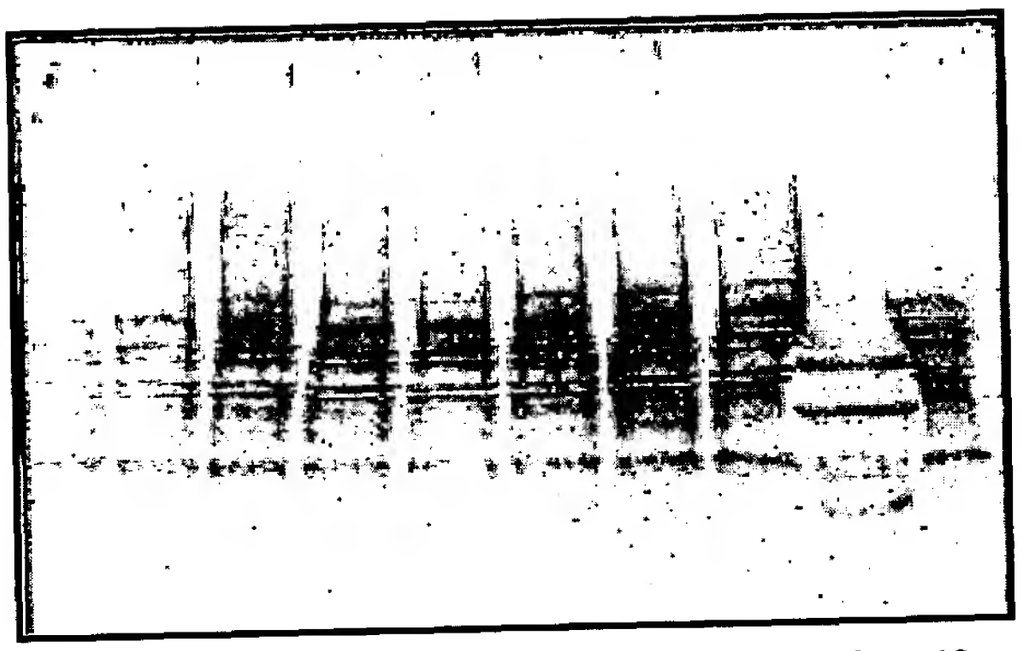

MW (Kd)
95
68
39
29
20
14
Lane 1 2 3 4 5 6 7 8 9 10
50%
25%
25%
MRAWIFFLLCLAGRALAAPQQEALAHSHRDFQPVL----------
Human BM40 Signal
Human Endostatin

Fig. 13